REMARKS/ARGUMENTS

Claims 1-28 remain pending. Favorable reconsideration is respectfully requested.

The present invention relates to a method for preserving an oxygen infusion comprising an aqueous suspension of molecular assemblies which contain hemoglobin or a heme compound, by

a) modifying the molecular assemblies with polyoxyethylene; and

b) converting the hemoglobin or the heme compound into a deoxy-form by removing oxygen from the suspension.

See Claim 1.

The present invention also relates to a method of producing an oxygen infusion comprising an aqueous suspension of molecular assemblies which contain hemoglobin or a heme compound, by

a) preparing a suspension of the molecular assembly containing the hemoglobin or the heme compound, the molecular assembly being modified with polyoxyethylene;

b) making the hemoglobin or the heme compound into a deoxy-form by removing oxygen from the suspension; and

c) packing the suspension containing the deoxy-form hemoglobin or heme compound, in an oxygen-impermeable container which is filled with an inert gas.

See Claim 16.

The present invention also relates to an oxygen infusion, comprising a suspension of molecular assemblies comprising hemoglobin or a heme compound, the assemblies being modified with polyoxyethylene; said hemoglobin or heme compound being in a deoxy-form.

See Claim 17.

An important feature of the claimed methods and oxygen infusion are the "molecular assemblies" recited in Claims 1, 16, and 17. As described in the present specification at page 7, lines 15-18:

> "the term 'molecular assembly' refers to an assembled structure constructed of molecules such as lipids and/or proteins, for example, not through covalent bonds but through interactions (such as hydrophobic interaction, electrostatic interaction and hydrogen bond) acting between the molecules in an aqueous medium."

Thus, based on that description the molecular assemblies of the present invention do not embrace a simple solution of hemoglobin.

The rejection of Claims 1-4, 6, 13-17, 21 and 26-28 under 35 U.S.C. §102(b) over Nho, WO 92/08478, is respectfully traversed. That reference fails to disclose the claimed methods and oxygen infusion.

Nho discloses a method of enhancing the long-term storage stability of hemoglobin products by gas exchange through a permeable membrane, in order to deoxygenate the product. See the Abstract. The hemoglobin product described in the reference may be hemoglobin in solution which may be chemically modified or which may not be chemically modified, or hemoglobin contained within living cells. See page 6, lines 21-24. At page 12, line 9 to page 13, line 6, Nho describes covalently modifying hemoglobin with polyoxyethylene, referred to as "PEG-Hb."

Hemoglobin in solution as disclosed by Nho is not used as part of a molecular assembly as recited in the claimed methods and infusion. Rather, that protein is simply present in solution and is not non-covalently associated with any other component in the solution, which is a required aspect of a molecular assembly. Accordingly, Nho fails to describe modification of molecular assemblies modified with polyoxyethylene as recited in

Claims 1, 16, or 17. Thus, the reference fails to describe the claimed methods or infusion. Withdrawal of this ground of rejection is respectfully requested.

Moreover, there is no suggestion in Nho to modify a molecular assembly as claimed. The reference explicitly describes using hemoglobin in solution that is not non-covalently associated with any other component in the solution. Therefore, one reading that reference would not be motivated to incorporate the hemoglobin into a molecular assembly. Nho also described using hemoglobin contained in living cells. However, one would not be motivated to treat the cells with polyoxyethylene because there is no reason to expect that hemoglobin in the cells would successfully react and the polyoxyethylene might be expect to harm the cells.

The rejection of Claims 1-20, 22-23 and 26-28 under 35 U.S.C. §102(b) over Sakai et al. (Bioconjugate Chemistry, vol. 11, pages 425-432) is respectfully traversed. Sakai et al. is not available as prior art against the present application.

Applicants submit herewith a copy of international application No. PCT/JP00/05512, and an English translation of the same. Applicants submit that the pending claims are supported by the international application. Accordingly, the claims of the present application are entitled to the August 17, 2000 filing date of the international application.

The publication date of Sakai et al. is April 21, 2000 (see the bottom of page 425: "Published on the Web 04/21/2000"). That reference names as authors the same inventors of the present application. Since (1) the effective U.S. filing date of the present application is less than one year after the publication date of Sakai et al. and (2) the authors of the reference are the same inventors of the present application, Sakai et al. is not available as prior art against the present application under 35 U.S.C. §102(a) or §102(b). Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of Claims 1-2, 5,13,15,17 and 22 under 35 U.S.C. §102(b) over Sakai et al. (abstract from Jinko Ketsueki, vol. 7, no. 4, pages 105-110, 1999), hereinafter referred to as Sakai et al. Abstract, is respectfully traversed. The Sakai et al. Abstract is not available as prior art against the present application.

The publication date of Sakai et al. Abstract is believed to be August 20, 2000. A copy of the reference is submitted herewith, with a date-stamp on the last page.

As discussed above, the effective filing date of the present application is August 17, 2000. Since Sakai et al. Abstract was published after the effective filing date of the present application, that reference is not available as prior art against the present application. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of Claims 7-12 and 18-20 under 35 U.S.C. §103(a) over Nho in view of Sakai et al. is respectfully traversed.

As discussed above, Sakai et al. is not available as prior art against the present application. Therefore, this rejection is unsustainable and should be withdrawn.

The rejection of Claim 5 under 35 U.S.C. §103(a) over Nho in view of Estep, WO 89/06969, is respectfully traversed. Those references fail to suggest the claimed methods and oxygen infusion.

As discussed above, Nho fails to describe modification of molecular assemblies modified with polyoxyethylene as recited in Claims 1, 16, or 17, and fails to suggest such modification.

Estep has been cited for its disclosure of incorporating a reducing agent into a solution of hemoglobin. See the Abstract. No evidence has been set forth that Estep suggests modifying a molecular assembly with polyoxyethylene.

Based on the foregoing, Nho in view of Estep fails to suggest the claimed methods and oxygen infusion. Accordingly, the claims are not obvious over those references. Withdrawal of this ground of rejection is respectfully requested.

The rejection of Claims 22-25 under 35 U.S.C. §103(a) over Nho in view of Applicants' allegedly admitted prior art in the specification is respectfully traversed.

As discussed above, Nho fails to describe modification of molecular assemblies modified with polyoxyethylene as recited in Claims 1, 16, or 17, and fails to suggest such modification.

The specification has been cited for its alleged disclosure of molecular assemblies. No evidence has been set forth that background information discussed in the specification suggests non-covalently modifying hemoglobin with polyoxyethylene.

Based on the foregoing, Nho in view of the discussion in the present application fails to suggest the claimed methods and infusion. Accordingly, the claims are not obvious over those references. Withdrawal of this ground of rejection is respectfully requested.

The objection to the Abstract and the rejection of the claims under 35 U.S.C. §112, second paragraph, are believed to be obviated by the amendment submitted above.

A substitute Abstract is submitted herewith. Claims 8 and 19 have been amended to specify that the molecular weight is in the units of Daltons. Claim 9 has been amended to explicitly recite that the molecular assemblies comprise lipid. In view of these amendments, withdrawal of the objection and the rejection is respectfully requested.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

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